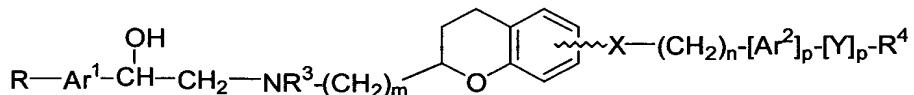


What is claimed as new and useful is:

1. A compound of the formula I:



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wherein

R is hydrogen, hydroxy, oxo, halo, C₁-C₁₀haloalkyl, C₁-C₁₀ alkyl, cyano, nitro, NR¹R¹, S R¹, OR¹, SO₂R², OCOR², NR¹COR², COR², NR¹SO₂R², NR¹CO₂R¹, pyrrole, or Ar², optionally substituted with hydroxy, halogen, cyano, NR¹R¹, SR¹, trifluoromethyl, OR¹, C₃-C₈ cycloalkyl, phenyl, NR¹COR², COR², SO₂R², OCOR², NR¹SO₂R², or NR¹CO₂R¹;

R^1 is hydrogen, C1-C10 alkyl optionally substituted with 1 to 4 substituents

selected from hydroxy, halogen, CO₂H, CO₂C₁-C₁₀ alkyl, SO₂C₁-C₁₀alkyl, C₁-C₁₀ alkoxy; or C₃-C₈ cycloalkyl, phenyl or naphthyl, each optionally substituted with 1 to 4 substituents selected from halogen, nitro, oxo, C₁- C₁₀ alkyl, C₁-C₁₀ alkoxy, and C₁-C₁₀ alkylthio;

R^2 is R^1 or NR^1R^1 ;



R^3 is hydrogen, C₁-C₁₀ alkyl or $R-Ar^1-CH-CH_2-$;

Ar^1 is $\text{Ar}^1\text{-O-CH}_2$, phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4

20 heteroatoms selected from O, S and N, each moiety being optionally fused to a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl ring or substituted with oxo;

m is 1, 2 or 3;

(CH₂)_m may be optionally replaced with C-O-(CH₂)_m;

X is SO_2 -piperiziny, NR^3-SO_2 , or SO_2-NR^3 .

n is 0, 1, 2, 3, or 4;

Ar² is phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each moiety being optionally substituted with halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, and OR, or being fused to a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl ring or optionally substituted with oxo;

Y is O - Y, NR¹, NR¹CO, C₃-C₈ cycloalkyl or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each of which is optionally substituted with oxo;

10 p is 0 or 1;

R⁴ is hydrogen, R¹, R², oxo, C₁-C₁₀ heteroalkyl, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, each being optionally substituted with C₃-C₈ cycloalkyl, phenyl, naphthyl, benzofuran, carbazole, dibenzothiophene, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S, and N, each ring structure being optionally substituted with halo and C₁-C₁₀ alkyl,

15

and pharmaceutically acceptable salts and esters thereof.

20

2. A compound of claim 1 wherein Ar¹ is optionally substituted phenyl or pyridyl, X is NR³-SO₂ or SO₂-NR³, Ar² is phenyl, pyridyl pyrimidinyl or pyrrolyl, Y is optionally substituted pyridyl, pyrrolyl, pyrimidinyl, quinolinyl, imidazolyl, and dihydrobenzofuran, and R⁴ is R¹ or optionally substituted C₁-C₁₀ alkyl.

25

3. A compound of claim 2 wherein m is one and n is zero or one.

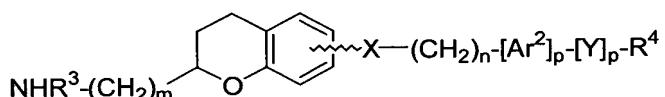
30

4. A compound of Claim 3 wherein R³ is hydrogen and R⁴ is C₁-C₁₀ alkyl optionally substituted with optionally substituted C₃-C₈ cycloalkyl, phenyl, or pyridyl.

5. A compound of claim 4 wherein R is hydrogen, halo, C₁-C₁₀ alkyl, nitro or NR¹R¹, n is zero, X is attached to the chroman moiety in the 6 position, n is zero, Ar² is phenyl or pyridyl, and Y is optionally substituted pyridyl or pyrrolyl.

6. A compound of Claim 1 wherein the -OH group of the compound of Formula 1 is in the R configuration.

7. A compound useful in the preparation of compounds of Formula 1 of the formula



30

Formula II/Compound 2

wherein,

R is hydrogen, hydroxy, oxo, halo, C₁-C₁₀haloalkyl, C₁-C₁₀ alkyl, cyano, nitro, NR¹R¹,
5 S R¹, OR¹, SO₂R², OCOR², NR¹COR², COR², NR¹SO₂R²,

NR¹CO₂R¹, pyrrole, or Ar², optionally substituted with hydroxy, halogen,
10 cyano, NR¹R¹, SR¹, trifluoromethyl, OR¹, C₃-C₈ cycloalkyl, phenyl,
NR¹COR², COR², SO₂R², OCOR², NR¹SO₂R², or NR¹CO₂R¹;

R¹ is hydrogen, C₁-C₁₀ alkyl optionally substituted with 1 to 4 substituents

selected from hydroxy, halogen, CO₂H, CO₂C₁-C₁₀ alkyl, SO₂C₁-C₁₀alkyl,
15 C₁-C₁₀ alkoxy; or C₃-C₈ cycloalkyl, phenyl or naphthyl, each optionally
substituted with 1 to 4 substituents selected from halogen, nitro, oxo, C₁- C₁₀
alkyl, C₁-C₁₀ alkoxy, and C₁-C₁₀ alkylthio;

R² is R¹ or NR¹R¹;



R³ is hydrogen, C₁-C₁₀ alkyl or R-Ar¹-CH-CH₂-;

m is 1, 2 or 3;

15 (CH₂)_m may be optionally replaced with C-O-(CH₂)_m;

X is SO₂-piperizinyl, NR³--SO₂, or SO₂—NR³;

n is 0, 1, 2, 3, or 4;

Ar² is phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4
heteroatoms selected from O, S and N, each moiety being optionally

20 substituted with halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, and OR, or being fused to
a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected
from O, S, and N, the fused heterocyclic ring being optionally used to a phenyl
ring or optionally substituted with oxo;

Y is O - Y, NR¹, NR¹CO, C₃-C₈ cycloalkyl or a 5 or 6 membered heterocyclic ring
25 with from 1 to 4 heteroatoms selected from O, S and N, each of which is
optionally substituted with oxo;

p is 0 or 1;

R⁴ is hydrogen, R¹, R², oxo, C₁-C₁₀ heteroalkyl, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl,
each being optionally substituted with C₃-C₈ cycloalkyl, phenyl, naphthyl,

benzofuran, carbazole, dibenzothiophuran, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S, and N, each ring structure being optionally substituted with halo and C₁-C₁₀ alkyl,

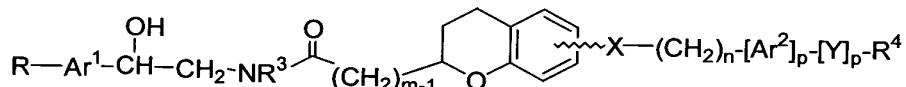
5 8. A compound of claim 7 wherein X is NR³-SO₂ or SO₂-NR³, Ar² is phenyl, pyridyl pyrimidinyl or pyrrolyl, Y is optionally substituted pyridyl, pyrrolyl, pyrimidinyl, quinolinyl, imadazolyl, and dihydrobenzofuranyl, and R⁴ is R¹ or optionally substituted C₁-C₁₀ alkyl.

9. A compound of claim 8 wherein m is one and n is zero or one.

10 10. A compound of Claim 9 wherein R³ is hydrogen and R⁴ is C₁-C₁₀ alkyl optionally substituted with optionally substituted C₃-C₈ cycloalkyl, phenyl, or pyridyl.

11. A compound of claim 10 wherein n is zero, X is attached to the chroman moiety in the 6 position, n is zero, Ar² is phenyl or pyridyl, and Y is optionally substituted pyridyl or pyrrolyl.

12. A compound useful in the preparation of compounds of Formula 1 of the formula



15 Formula III/Compound 34

wherein

R is hydrogen, hydroxy, oxo, halo, C₁-C₁₀haloalkyl, C₁-C₁₀ alkyl, cyano, nitro, NR¹R¹, S R¹, OR¹, SO₂R², OCOR², NR¹COR², COR², NR¹SO₂R²,

20 NR¹CO₂R¹, pyrrole, or Ar², optionally substituted with hydroxy, halogen, cyano, NR¹R¹, SR¹, trifluoromethyl, OR¹, C₃-C₈ cycloalkyl, phenyl, NR¹COR², COR², SO₂R², OCOR², NR¹SO₂R², or NR¹CO₂R¹;

R¹ is hydrogen, C₁-C₁₀ alkyl optionally substituted with 1 to 4 substituents

25 selected from hydroxy, halogen, CO₂H, CO₂C₁-C₁₀ alkyl, SO₂C₁-C₁₀alkyl, C₁-C₁₀ alkoxy; or C₃-C₈ cycloalkyl, phenyl or naphthyl, each optionally substituted with 1 to 4 substituents selected from halogen, nitro, oxo, C₁- C₁₀ alkyl, C₁-C₁₀ alkoxy, and C₁-C₁₀ alkylthio;

R² is R¹ or NR¹R¹;



R³ is hydrogen, C₁-C₁₀ alkyl or R-Ar¹-CH-CH₂-;

Ar¹ is Ar¹-O-CH₂, phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4

heteroatoms selected from O, S and N, each moiety being optionally fused to a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl ring or substituted with oxo;

5 m is 1, 2 or 3;

$(CH_2)_m$ may be optionally replaced with C-O-($CH_2)_m$;

X is SO_2 -piperizinyl, NR^3-SO_2 , or SO_2-NR^3 ;

n is 0, 1, 2, 3, or 4;

10 Ar^2 is phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each moiety being optionally substituted with halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, and OR, or being fused to a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl ring or optionally substituted with oxo;

15 Y is O - Y, NR^1 , NR^1CO , C₃-C₈ cycloalkyl or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each of which is optionally substituted with oxo;

p is 0 or 1;

20 R^4 is hydrogen, R^1 , R^2 , oxo, C₁-C₁₀ heteroalkyl, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, each being optionally substituted with C₃-C₈ cycloalkyl, phenyl, naphthyl, benzofuran, carbazole, dibenzothiophene, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S, and N, each ring structure being optionally substituted with halo and C₁-C₁₀ alkyl.

25 13. A compound of claim 12 wherein Ar^1 is optionally substituted phenyl or pyridyl, X is NR^3-SO_2 or SO_2-NR^3 , Ar^2 is phenyl, pyridyl pyrimidinyl or pyrrolyl, Y is optionally substituted pyridyl, pyrrolyl, pyrimidinyl, quinolinyl, imidazolyl, and dihydrobenzofuran, and R^4 is R^1 or optionally substituted C₁-C₁₀ alkyl.

14. A compound of claim 13 wherein m is one and n is zero or one.

30 15. A compound of Claim 14 wherein R³ is hydrogen and R⁴ is C₁-C₁₀ alkyl optionally substituted with optionally substituted C₃-C₈ cycloalkyl, phenyl, or pyridyl.

16. A compound of claim 15 wherein R is hydrogen, halo, C₁-C₁₀ alkyl, nitro or NR¹R¹, n is zero, X is attached to the chroman moiety in the 6 position, n is zero, Ar² is phenyl or

pyridyl, and Y is optionally substituted pyridyl or pyrrolyl.

17. A method of treating a beta-3 adrenergic receptor mediated condition which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of Formula 1, or a salt or ester thereof.

5 18. A method of treating a beta-3 adrenergic receptor mediated condition which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 9, or a salt or ester thereof.

10 19. A method of treating obesity in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of Formula 1, or a salt or ester thereof.

20. A method of treating obesity in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 9, or a salt or ester thereof.

15 21. A method of treating diabetes in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of Formula 1, or a salt or ester thereof.

22. A method of treating diabetes in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 9, or a salt or ester thereof.

20 23. A pharmaceutical composition comprising an effective amount of a compound of Formula 1 or a pharmaceutically acceptable salt thereof in combination with a pharmaceutically acceptable carrier.

24. A composition comprising an effective amount of a compound of Formula 1, or a salt hereof, in combination with an inert carrier.